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AN INFUSION DEVICE FOR MEDICAL USE

DESCRIPTION

Background of the Invention.

The present invention relates to an infusion device for medical use.

In particular, the device of the invention is used in apparatus for the extracorporeal treatment of blood, for example apparatus for dialysis and/or plasmapheresis, in order to provide an infusion line which can be connected to an extracorporeal blood circuit associated with the aforementioned apparatus; the device in question can also be used for forming an infusion line which can be connected directly to the patient's vascular system.

As is known, a conventional infusion line comprises at least one length of tubing designed to connect a bag containing a specified infusion liquid to an extracorporeal blood circuit or directly to a patient through conventional access means such as needles, catheters or the like.

A pump, of the peristaltic type for example, can be provided on the infusion line for moving the infusion fluid in the desired way. For example, United States Patent No. 5,698,090 in the name of Hospal Industrie describes an infusion line comprising a bag containing a replacement liquid, associated for operation with a balance designed to measure the weight of the bag and send a corresponding electrical signal to a control unit.

The control unit also acts on a peristaltic pump positioned on the infusion line; in particular, the unit controls the angular velocity of the pump in a suitable way according to the difference between the actual consumption signalled by the balance and the value set by the user.

Downstream of the peristaltic pump, the infusion line is connected to a collection chamber in which the infusion liquid can be combined with the blood obtained from a venous branch of an extracorporeal blood circuit.

Downstream of the aforesaid chamber, the blood, having been enriched with the infusion liquid, is returned to the patient's cardiovascular system.

The device described above can be used to control the actual flow and consequently the velocity of the infusion pump, and to achieve a separation of liquid and air such that the propagation of dangerous gas particles towards the patient is prevented.

Because of the presence of the balance and the control unit, if the total contents of liquid in the bag are known, the pump can be stopped and the suction of air bubbles from the bag prevented when the condition is reached in which the liquid in the bag has been used up.

However, it should be noted that there is an intrinsic minimum time interval between the actual emptying of the bag and the detection of this situation by the system consisting of the balance combined with the control unit. Consequently, in order to ensure the reliable operation of the described system, it is necessary to have a collection chamber (often referred to as a "bubble trap") in the infusion line, in which a specified volume of liquid can be held constantly; in normal operating conditions, the collection chamber holds this specified volume of fluid and enables the control system and balance to have sufficient time to detect when the end of infusion condition has actually been reached.

It should be noted that the detection of an end of infusion condition at the correct time is also important for the purpose of avoiding a discrepancy between the prescribed amount of infusion liquid for the patient and the actual infusion provided by the machine.

In addition to the solution described above, in which a balance is used to detect the end of infusion condition, widespread use has also been made in the past of solutions using level sensors, of the optical and/or ultrasonic type for example, which can interact with an infusion liquid collecting chamber, typically located in an intermediate area of the infusion line.

In the presence of a specified flow of liquid from the bag, the infusion liquid collecting chamber forms a liquid level and a reservoir for separating any air bubbles.

A level sensor associated with the chamber can be used to check and detect any fall in the level, permitting immediate recognition of a danger condition caused by the end of the supply of infusion liquid.

Clearly, if they are to operate correctly, the level sensors described above for detecting any fall in level or the presence of air bubbles in the flow directed towards the patient also require the presence of a collection chamber in the infusion line, for the formation of a level which will be detectable.

In other words, according to the known technical solutions, in order to enable an end of infusion condition to be detected and to ensure the reliable separation of air from the fluid directed towards the patient, it is necessary to provide a proper collection chamber or drip chamber in the infusion line, where the infusion fluid can accumulate, thus considerably reducing its velocity.

In practice, the collection chamber has a radial dimension considerably greater than that of the infusion tube, and, in the manufacturing process, is typically made separately from the rest of the line. The various lengths of tubing forming the infusion line and the collection chamber then undergo a rather complicated assembly process which considerably increases the total costs of the infusion line.

Furthermore, in the case of infusion lines interacting with level sensors, it is necessary to use optical or acoustic detectors which further increase the weight of the structure of the device. The control system has to be programmed to coordinate and control the signals received from the sensors.

Finally, all the known devices require the presence, downstream of the pump, of at least one safety valve, for example a clamp, which can close the tubing as soon as the condition of the end of infusion or the approaching end of infusion is detected.

Clearly, the fluid collection chamber can separate air from the liquid only when a minimum quantity of liquid is present in the chamber: if the liquid in the collection chamber is used up (this inevitably occurs after a certain time when the infusion liquid has been used up, unless the infusion pump is stopped at the correct time), there will be a transfer of gas towards the patient.

Finally, it should also be mentioned that there are known air-liquid separators of the type comprising a containing body forming two adjacent chambers separated by a hydrophilic membrane; the containing body has an inlet aperture for a fluid comprising liquid and gas particles. The liquid can pass through the hydrophilic membrane and emerge through an outlet aperture. The gas which reaches the first chamber is discharged through secondary apertures positioned upstream of the

hydrophilic membrane, at least one hydrophobic membrane being used at these apertures to prevent the liquid from passing through.

The device which has been described allows the fluid, containing gas particles, to be separated into two parts, namely a liquid portion which emerges from the outlet aperture provided in the second chamber, and a gas portion which is released through the secondary apertures provided in the first chamber.

It should be noted that the air separator device which has been described does not require a constant presence of liquid stagnating within it in order to separate the gas; in other words, the fluid passing through the separation device is continuously divided into liquid, which continues along the line, and gas, which is discharged to the exterior.

Summary of the Invention.

In this situation, the object of the present invention is to provide a novel infusion device for the infusion of a liquid from a bag using a line having a very simple structure and overcoming all the drawbacks described above.

In particular, an object of the present invention is to provide an infusion device which does not require the use of a chamber for collecting the fluid upstream of the infusion point, and which does not require the presence of any optical or ultrasonic level sensor.

In particular, an object of the present invention is to combine efficiently, in an infusion line, the presence of a balance operating on the infusion bag with the presence of a special system capable of continuously preventing the passage of air to the patient during the detection of the end of infusion condition, in such a way as to make the whole infusion line extremely simple, efficient and reliable, so that there is theoretically no need to have further safety systems (clamps or other devices) for stopping the flow along the line.

Finally, an object of the present invention is to provide an infusion line which allows a plurality of bags to be incorporated, with a simple means of changing from one bag to the next when the liquid contained in each infusion bag is used up.

These and other objects, which will be made clearer in the following description, are essentially achieved by an infusion device according to the descriptions in one or more of the attached claims.

Further characteristics and advantages will be made clearer by the detailed description of a preferred, but not exclusive, embodiment of an infusion device according to the present invention.

Brief Description of the Drawings.

This description is provided below with reference to the attached drawings, provided solely for guidance and therefore without restrictive intent, in which:

- Figure 1 is a schematic view of an infusion device according to the invention, applied to an extracorporeal blood circuit;
- Figure 2 shows a portion of the device of Figure 1, comprising a support element and a curved length of tubing;
- Figure 3 is a view similar to that of Figure 2, in which part of the support element has been removed to show its internal structure more clearly;
- Figure 4 is a detail view of a support element forming part of the device according to the invention;
- Figure 5 is a section taken through the line V-V of Figure 4;
- Figure 6 shows the part of the support element which is removed in the view of Figure 3;
- Figure 7 is a second embodiment of a support element according to the invention, which can be used in substitution for the support element of figure 2;
- figure 8 is a view from above of figure 7;
- figure 9 is the same view as in figure 7, with some parts removed better to evidence others;
- figure 10 is a view from above of figure 9;

- figure 11 is a section according to line XI-XI of figure 7;
- figure 12 is a section according to line XII-XII of figure 7;
- figure 13 is a section according to line XIII-XIII of figure 12;
- figure 14 is a view from inside of a part of the support element which is removed from view in figure 9.

Detailed Description.

With reference to the attached figures, a description will be given of an infusion device 3 according to the invention.

The device 3 has an infusion line 2 and at least one container 4 designed to hold a specified quantity of a liquid to be infused into a patient; in particular, the infusion point 5 can be positioned in a specified area of an extracorporeal blood circuit, or, alternatively, can be connected directly to the patient.

The device 3 can also comprise a plurality of containers 4, which can be sequentially brought into fluid communication with the infusion point by opening and closing corresponding shut-off elements 6, such as clamps or the like, which may be manually or automatically operated.

A weighing device 7, such as a balance, is associated for operation with the infusion liquid container or containers, to detect the total weight of the container or containers and send a corresponding control signal. In practice, the control signal is a signal related to the total weight measured by the balance during the treatment.

This signal is transmitted to a control unit 8 associated with the weighing device; the control unit 8 can sample and store the weight measured by the balance at finite time intervals, for example at regular intervals. Thus the control unit 8 can determine the actual flow passing through the infusion line 2 and suitably adjust movement means associated with the line whenever a discrepancy is found between the actual flow and the desired flow.

It should be noted that the movement means can comprise at least one pump, for example a peristaltic pump 9, or, in the case of gravity operation for example, a flow control valve, for example an electromagnetic clamp.

Typically, the desired flow can be set by the user or pre-programmed in the control unit and, in any case, can be a value which is constant or variable over time. The control unit 8 can determine the decrease in the actual weight of the infusion liquid container, and can adjust the movement means, if necessary, to obtain the desired flow along the line.

When the total weight of the content of each container is known, the control unit 8 can also detect at least a condition of emptying or end of infusion, and activate a corresponding control procedure. This procedure can comprise a stage of commanding the movement means (peristaltic pump 9) to stop the transport of fluid along the line and/or a stage of signalling that the container is empty or that a specified volume of liquid has been used up.

If the infusion device 3 comprises two or more liquid containers 4, the infusion line 2 will also have a plurality of branches 2a, each designed to bring a corresponding container into fluid communication with a common part 2b of the line 2 and thus with the infusion point 5. In this case, each branch 2a has a flow shut-off element 6 which can be switched between an open and a closed position, to selectively permit or prevent the passage of fluid.

The flow shut-off elements 6 can be activated manually or commanded sequentially by the control unit 8. For example, the control unit 8 can be programmed so that, when an empty condition of a container 4 is detected, it can command the closing of the shut-off element 6 located in the branch 2a related to the empty container 4, and the opening of one of the shut-off elements 6 located in a branch 2a corresponding to a container in which liquid is present. This procedure can be repeated until all the containers have been emptied.

The device in question comprises a continuous fluid separator 10, located in the infusion line 2, for separating the fluid supplied from the container or containers 4 into a gas portion and a liquid portion; this continuous separator 10 can allow only the liquid to continue along the infusion line, while separating and discharging towards the exterior any gas bubbles supplied from the container 4.

In particular, when the infusion liquid in a container 4 has been used up, the separator 10 receives any gas and discharges it to the exterior, thus preventing the passage of gaseous substances downstream of the section in which this separator operates.

The continuous separator 10 comprises a containing body 11 having at least one inlet 12 for receiving a fluid supplied from the container, at least one first outlet 13 for receiving a liquid portion of the flow and sending it downstream of the selector to the infusion point 5, at least one second outlet 14 for receiving the gaseous portion of the fluid and discharging it towards the exterior, and selector means 15 interposed between the inlet 12 and the first outlet 13 and capable of continuously separating the fluid into a gaseous portion and the liquid portion.

The selector means 15 comprise at least one hydrophilic membrane 16 having one side 16a facing the first outlet 13 and one side 16b facing the inlet 12 for receiving the fluid and transferring only liquid towards the first outlet; the selector means 15 also comprise at least one hydrophobic membrane 17 having one side 17a facing the second outlet 14 and one side 17b facing the inlet 12 to receive the fluid and transfer only gas towards the second outlet 14.

With reference to the extension of the infusion line, the separator 10 is interposed between the movement means (peristaltic pump 9) and the infusion point 5, and, in particular, is positioned immediately downstream of the movement means.

As can be seen in the attached figures 1 to 6, the device 3 comprises a rigid support element 1, holding opposing portions of a first length of tubing 18 of the line 2 and specifically designed to interact with the movement means (peristaltic pump 9). In practice, the rigid support 1 holds the first length of tubing 18 in such a way that this first length has a curved shape and a specified axial extension.

The support element 1 is positioned transversely with respect to the mid-line axis of the opposing portions of the first length of tubing 18, and enables the line to be manipulated easily to allow the first length 18 to be easily fitted around a rotor of a peristaltic pump 9.

Upstream of this first length of tubing 18, the infusion line comprises a second length of tubing 19 extending between the container 4 and the rigid support 1 and placed in fluid communication with the first length 18. As mentioned, the second length of tubing 19 can consist of a single duct connected to a single liquid container 4, or can branch terminally into a plurality of branches 2a, each connected to a corresponding container 4.

A description will now be given of the detailed structure of the rigid support element 1 (figures 1 to 6), which comprises a first lateral portion 20, forming the containing body 11, and a second lateral portion 22, of tubular profile, to which are fixed corresponding ends of the first and the second lengths 18 and 19 of the infusion line 2; the second lateral portion 22 and the first lateral portion 20 are connected rigidly together by a rigid cross-piece 23 provided with at least one through hole 24 which can act as an element for attaching the rigid support 1 to a support wall which is not illustrated; the rigid cross-piece 23 is essentially flat and parallel to a plane in which the first length of tubing 18 lies.

The containing body 11 formed by the first lateral portion 20 comprises a base 25 and a cover portion 26, which interact with each other to form a passage 27 for fluid between the inlet 12, on the one hand, and the first and second outlets 13, 14, on the other hand.

More precisely, the base 25 forms a through channel 28 for putting the passage 27 in fluid communication with the exterior. This through channel 28 extends orthogonally to the plane in which the support element 1 lies, and is located in the proximity of a peripheral area of the base 25; thus, when the infusion device 3 is mounted on the peristaltic pump 9 in operating conditions, the through channel 28 is located in a topmost area of the base 25.

As will be seen in Figure 5, the fluid passage 27 within the containing body 11 is essentially divided by the hydrophilic membrane 16 into two half-parts or chambers 27a and 27b. Because of its special positioning, the through channel 28 is located in the uppermost point of the chamber 27a (located upstream with respect to the direction of flow) into which the passage 27 is divided, in order to discharge any gas efficiently. For this purpose, the hydrophobic membrane 17 operates in an inlet section of the through channel 28 facing the interior of the containing body 11.

With reference to Figure 5 again, it will be noted that the base 25 comprises an incorporated first tubular connecting element 29 for receiving one end of the first length of tubing 18. In turn, the cover portion 26 comprises an incorporated second tubular connecting element 30 having an axis of extension inclined with respect to that of the first tubular element 29.

The second connecting element 30, for example a Luer connector, can be connected directly to a T-shaped connector of an extracorporeal blood circuit 33, upstream or downstream of a blood treatment unit 34 (a dialysis filter or other device). Thus, since a direct connection to the extracorporeal blood circuit 33 is possible, it becomes unnecessary to have a tube downstream of the separator 10; this provides the advantage of preventing any possible involuntary blockage which would be difficult to detect by means of the sensor system associated with the extracorporeal circuit 33.

It should be noted in this context that any infusion liquid transport tube located downstream of the separator 10 would, if the tube were blocked, cause a pressure stress for a certain period of time, affecting the separator 10 and the membranes 16 and 17 in particular, as well as the liquid seals.

It should also be noted that the rigid support 1 is thin, so that the whole infusion line 2 can occupy very small volumes.

Nevertheless, the efficiency of the system is not reduced, because of the particular structure of the containing body 11 and the positions of the membranes 16 and 17; in particular, the hydrophilic membrane 16 is interposed between the base 25 and the cover portion 26, and extends essentially through the whole containing body 11; the base 25 and the cover portion 26 comprise corresponding base walls 25a and 26a and corresponding perimeter edges 25b and 26b emerging from the base walls 25a and 26a to form the passage through which the fluid is transported.

The hydrophilic membrane 16 extends parallel to the base walls 25a and 26a in a position spaced from the walls, thus providing an active surface essentially equal to the area of the containing body 11 seen in plan view.

It should also be noted that the containing body 11 has a plurality of projections 31 and 32 emerging from the base wall 25a of the base and from the base wall 26a of the cover portion.

In detail, the projections 31 associated with the base 25 comprise teeth distributed uniformly over the surface of the base wall 25a of the base, while the projections 32 associated with the cover portion 26 comprise angularly spaced deflectors for guiding the liquid flow towards the first outlet 13.

In terms of construction, the base 25 of the containing body, the rigid cross-piece 23 and the second lateral portion 22 are made in a single piece, while the cover portion 26 is fixed to the base 25 after the hydrophobic and hydrophilic membranes 17 and 16 have been placed in position.

Figures from 7 to 14 illustrate a second embodiment of a rigid support element which can be used alternatively to the rigid support element of the first embodiment, described above. In the second embodiment, as in the first, the support element is associable to an infusion device 3, such as the infusion device 3 shown in figure 1, and engages opposite portions of the first length of tubing 18 of the infusion line 2, as well as a portion of end of the second length of tubing 19.

For reasons of simplicity and greater clarity, in figures from 7 onwards the support element is denoted by 1, like the support element of the first embodiment, illustrated in figures from 1 to 6. Also, in figures from 7 onwards, the elements in the second embodiment which are similar both structurally and functionally to elements of the first embodiment, are denoted by the same numbers as in figures from 1 to 6.

In the second embodiment, the continuous fluid separator 10 includes a check valve 36 which is predisposed to prevent back-flow in an opposite direction to the flow direction of the extracorporeal fluid.

The check valve 36, or one-way valve, is predisposed along the liquid portion line after the liquid has already been separated from the gas portion by the continuous fluid separator 10. The check valve 36 is arranged internally of the separator containing body 11, in a zone comprised between the separator selector means 15 and the first outlet 13 (liquid outlet).

The check valve 36 comprises a mobile obturator organ 37 operating on a liquid passage mouth 35, through which the liquid portion passes. The obturator organ 37 is disc-shaped and is made of an elastomer material (for example silicone). The obturator organ 37 is mobile inside a chamber which, when the obturator is open, communicates on one side thereof with the fluid passage mouth 35. In the presence of a flow in the opposite direction to the desired direction, i.e. from the infusion point towards the separator 10, the obturator organ 37 automatically shuts the liquid passage mouth 35, interrupting the back-flow, so that the fluid in the extracorporeal circuit 33 cannot reach the separator 10.

The chamber housing the obturator organ 37 also communicates, with no possibility of shutting-off by the obturator, with the separator first outlet 13, on the opposite side to the liquid passage mouth 35. The check valve 36 is provided with means for preventing the obturator 37 from closing communication with the first outlet 13. The means for preventing are in the present embodiment constituted by at least one projection 38 which emerges from at least one wall delimiting the chamber containing the obturator 37, which projection 38 can interact contactingly with the obturator 37. In the illustrated embodiment a plurality of projections 38 are present, arranged in spoke fashion, each L-shaped and cooperating to contain the obturator 37 laterally.

The liquid passage mouth 35 is associated to the cover portion 26 of the containing body 11. In particular, the passage mouth 35 is arranged on the base wall 26a of the cover portion 26, which the hydrophilic membrane 16 faces at a distanced position therefrom.

As in the first embodiment, the containing body 11 internally affords a fluid passage 27 between the inlet 12 and the first outlet 13. This fluid passage 27 has an upstream portion 27a, comprised between the inlet 12 and the hydrophilic membrane 16, and a downstream portion 27b, comprised between the hydrophilic membrane 16 and the first outlet 13. The base wall 26a, on which the passage mouth 35 is afforded, delimits the downstream portion 27b of the fluid passage.

The passage mouth 35 is situated in a lateral end zone of the base wall 26a (see figure 14), which lateral end zone is opposite to the lateral end position in which the fluid inlet 12 is situated in the containing body 11.

The projections 32, arranged on the internal side of the base wall 26a, are subdivided into a first group of projections, which reach as far as the passage mouth 35, where the projections 32 are conformed in lines, parallel to one another and extending in a horizontal direction towards the passage mouth 35, defining a plurality of parallel linear conduits oriented in the direction of the liquid portion pathway; and into a second group of projections, arranged beyond the passage mouth 35, in which the projections 32 are like teeth, serrated and shaped as points or small segments, and are oriented tangentially with respect to the centre of the passage mouth 35.

The first outlet 13 is arranged at an upper end of an L-shaped outlet conduit 21. The upper end has an inclined axis with respect to the lie plane of the support element 1. The outlet conduit 21 is solidly associated to the cover portion 26 of the containing body.

The hydrophobic membrane 17, which operates on the second outlet 14 (vent) is situated in an upper zone of the upstream portion 27a of the fluid passage, where the term upper is used in reference to a use configuration in which the lie plane of the first U-shaped length of tubing 18 is vertical. In the use configuration the hydrophobic membrane 17 is situated at the highest point of the upstream portion 27a, and faces upwards.

In the use configuration, the hydrophobic membrane 17 has a horizontal lie plane, while the hydrophilic membrane 16 has a vertical lie plane. The hydrophobic membrane 17 is situated above the highest point of the operative filtering surface of the hydrophilic membrane 16. The hydrophilic membrane operative filtering surface does not comprise the perimeter edge of the hydrophilic membrane 16, which is constrained between the perimeter edges of the base 25b and the cover portion perimeter edges 26b.

The upstream portion 27a of the fluid passage has a flat conformation, with one dimension being smaller than the other two, with a lie plane that is parallel to the hydrophilic membrane 16, and thus vertical in the in-use configuration. The upstream portion 27a of the fluid passage has a fluid inlet which is arranged in a lower end zone of the upstream portion 27a itself, on an opposite side to the upper second outlet 14 for gas, where the hydrophobic membrane 17 is operative.

The passage section of the upstream portion 27a of the fluid passage increases gradually going from bottom to top, in the direction of the hydrophobic membrane 17, and then towards the second outlet 14. An upper end zone of the upstream portion 27a, superiorly delimited by the hydrophobic membrane 17, is located above the upper edge of the hydrophilic membrane operative filtering surface.

In the second embodiment, the through channel 28, which places the upstream portion 27a of the fluid passage 27 in communication with the outside atmosphere, through the hydrophobic membrane 17, has a longitudinal axis which extends parallel to the lie plane of the support element 1, and is afforded in a wing 26c of the cover portion 26. The wing 26c projects from an upper end of the cover portion

26, in a transversal direction to the direction of the lie plane of the main body of the cover portion 26.

The through channel 28 can be made, as in the illustrated embodiment, in the form of a plurality of uniformly-distributed vertical-axis holes.

The hydrophobic membrane 17 is kept in position thanks to a perimeter edge, constrained between an upper mouth of the base 25 and the wing 26c of the cover portion 26.

The base wall 25a of the base, which delimits the upstream portions 27a, has an inclined central part which is arranged at the vertical of the second outlet 14. Thanks to this inclination, the upstream portion 27a of the fluid passage has a central zone, arranged below the vertical of the second outlet 14, having a passage section which increases going from the bottom towards the top thereof. The height of the projections 31 (cooperating with the projections 32 to prevent excessive deformation of the filtering hydrophilic membrane 16) also increases in an upwards direction in this central zone.

In this central zone, the projections 31 are tooth-shaped, and are staggered among themselves with in a horizontal direction. The teeth, for example, can be pointed, aligned in vertical rows, or can be in short segments arranged vertically according to a plan view (figure 9); in a lateral end zone, close to the separator fluid inlet 12, the projections 31 are horizontally-arranged lines (on the right in figure 9); in another lateral end zone, opposite the fluid inlet, the projections 31 are C-shaped, arranged concentrically one inside another and with the arms of the C-shape elongate in a horizontal direction (on the left in figure 9).

The linear projections 31 define linear conduits, which direct the fluid towards the central zone of the upstream portion 27a, lying below the second outlet 14. The C-shaped projections 31 define C-shaped conduits which lead the fluid towards the central zone.

The projections 31 and 32 define two rest planes for both opposite sides 16b and 16a of the hydrophilic membrane, enabling deformations of the membrane in both directions to be limited.

The special arrangement and conformation of the upstream portion 27a, as well as the special arrangement and conformation of the second outlet 14 and the fluid inlet 12, contribute to improving the efficiency of the gas elimination from the fluid, while occupying only a relatively compact space.

In the second embodiment, the containing body 11 is incorporated in the support element 1 and develops prevalently in a transversal direction, from the first lateral portion 20 to the second lateral portion 22. The fluid inlet 12 is situated in the first lateral portion 20, while the first outlet 13, for liquid only, is located in a lateral end zone of the above-mentioned transversal development, beyond the median line of the development and in proximity of the second lateral portion 22. This enables the hydrophilic membrane 16 to have a large active filtration surface, and exploits to the full the space on the rigid cross-piece 23 without increasing the overall mass of the support element 1.

The second outlet 14, for gas (vent), is arranged in an intermediate zone of the transversal development of the containing body 11.

The check valve 36 predisposition prevents back-flow: in particular, the check valve 36 is a guarantee against any risk of passage of blood from the extracorporeal circuit 33 to the infusion line 2. The risk is particularly high in a case where the peristaltic pump 9, for any reason, loses its occluding capacity, i.e. the function of shutting off the first length of tubing 18, by effect of the squeezing of the flexible walls of the tubes in the contact zone between the tubes and the pump rollers. In the absence of this occluding function, blood might flow from the extracorporeal circuit 33, through the infusion line and even up to the containers 4, seriously injuring the patient.

Furthermore, using the check valve 36 prevents inlet of small quantities of blood coming from the extracorporeal circuit 33 into the infusion line 2, in particular the zone thereof comprised between the peristaltic pump 9 and the infusion point 5. This situation might occur due to the operating mode of the peristaltic pump 9, which causes an inconstant pressure in the infusion line 2, with the risk of possible blood leaks during the phase of operation in which the pressure drops.

The continuous fluid separator 10 of air and liquid, which has been described in two possible embodiments, is incorporated into a support element 1, predisposed to support a first length of tubing 18, in fluid connection with a second length of

tubing 19, also constrained to the support element 1, included in an infusion line 2 which is part of an infusion device 3.

In a further embodiment, not illustrated, of an infusion device according to the present invention, the check valve 36 can be not incorporated with the air-liquid separator, but can instead be included in the infusion line, located at a distance after the separator.

Also possible is the use of a gas-liquid separator, structured as the ones described herein above, not necessarily incorporated in the support element 1 but independent thereof, and inserted in a fluid transport line, which can be different from the one described herein above, for de-aerating the fluid conveyed.

Legend:

1	support element
2	infusion line
2a	branches of infusion line
2b	common part of infusion line
3	infusion device
4	containers
5	infusion point
6	flow shut-off elements
7	weighing device
8	control unit
9	peristaltic pump
10	continuous fluid separator (or deaerator device)
11	separator containing body
12	separator inlet (fluid inlet)
13	separator first outlet (liquid outlet)
14	separator second outlet (gas outlet)
15	separator selector means
16	hydrophilic membrane (liquid portion passage)
16a	hydrophilic membrane side facing liquid outlet
16b	hydrophilic membrane side facing fluid inlet
17	hydrophobic membrane (gas portion passage)
17a	hydrophobic membrane side facing gas outlet
17b	hydrophobic membrane side facing fluid inlet

18	first length of tubing (pump segment)
19	second length of tubing
20	first lateral portion of support element
21	outlet conduit
22	second lateral portion of support element
23	rigid cross-piece of support element
24	through hole of support element
25	base of containing body
25a	base wall of base
25b	perimeter edge of base
26	cover portion of containing body
26a	base wall of cover portion
26b	perimeter edge of cover portion
26c	upper transversal wing
27	fluid passage within containing body
27a	fluid passage half-part upstream hydrophilic membrane
27b	fluid passage half-part downstream hydrophilic membrane
28	through channel within containing body
29	first tubular connecting element
30	second tubular connecting element
31	projections associated to containing body base
32	projections associated to containing body cover portion
33	extracorporeal blood circuit
34	blood treatment unit
35	liquid passage mouth
36	check valve
37	mobile obturator organ
38	check valve projections

CLAIMS

1. An infusion device for medical use, comprising:

- at least one container (4) designed to hold a specified quantity of a liquid to be infused into a patient;
- a weighing device (7) associated for operation with the said container to measure the weight of the container and emit a corresponding control signal;
- a transport line (2) connected to the said container to convey the liquid, in operating conditions, towards an infusion point (5);
- means (9) for moving a flow of the liquid along the said line;
- a control unit (8) associated with the said weighing device and with the said movement means, the control unit receiving the said control signal and being capable of detecting at least one end of infusion condition;

the said infusion device being characterised in that it comprises a continuous fluid separator (10) capable of separating the fluid into a gaseous portion and a liquid portion, the said separator (10) operating in the said transport line (2).

2. The device of Claim 1, characterised in that the said separator comprises a containing body (11) having:

- at least one inlet (12) for receiving a fluid from the said container;
- at least a first outlet (13) for receiving a liquid portion of the said fluid;
- selector means (15) interposed between the said inlet and the said first outlet and capable of continuously separating the said fluid into a gaseous portion and a liquid portion.

3. The device of Claim 2, characterised in that the said containing body (11) of the separator comprises at least a second outlet (14) for receiving the said gaseous portion of the said fluid.

4. The device of Claim 2 or 3, characterised in that the said selector means comprise at least one hydrophilic membrane (16) having one side facing the said first outlet and one side facing the said inlet, for receiving the said fluid and transferring only liquid towards the said first outlet.

5. The device of Claim 3 or 4, characterised in that the said selector means comprise at least one hydrophobic membrane (17) having one side facing the said second outlet and one side facing the said inlet, for receiving the said fluid and transferring only gas towards the said second outlet.

6. The device of any one of Claims 1 to 5, characterised in that the said separator (10) is interpositioned between the said movement means (9) and the said infusion point (5).

7. The device of any one of Claims 1 to 6, characterised in that the said separator (10) is positioned immediately downstream of the said movement means (9).

8. The device of any one of Claims 1 to 7, characterised in that it comprises a rigid support (1) holding opposite ends of a first length of tubing (18) of the said line (2) designed to interact with the said movement means (9), the said first length of tubing having a curved shape and a predetermined axial extension.

9. The device of Claim 8, characterised in that the said line (2) comprises a second length of tubing (19) extending between the said container (4) and the said rigid support (1) and put into fluid communication with the said first length.

10. The device of Claim 8 or 9, characterised in that the said rigid support (1) comprises a first lateral portion (20) forming the said containing body (11).

11. The device of Claim 10, characterised in that the said rigid support (1) comprises a second lateral portion (22) with a tubular profile to which are fixed corresponding ends of the said first and the said second length of tubing of the said line (18, 19), the said second lateral portion being distanced from the said first portion (20).

12. The device of any one of Claims 3 to 11, characterised in that the said containing body (11) comprises a base (25) and a cover portion (26), interacting with one other to form a passage (27) for fluid between the said inlet (12) and the said first and second outlets (13, 14).

13. The device of Claim 12 and of any one of Claims 5 to 11, characterised in that the said base (25) forms a through channel (28) for putting the said passage (27) into fluid communication with the exterior, the said hydrophobic membrane (17) operating in the said channel.

14. The device of Claim 12 or 13, characterised in that the said base (25) comprises an incorporated first tubular connecting element (29).

15. The device of Claim 14, characterised in that the said cover portion (26) comprises an incorporated second tubular connecting element (30) having an axis of extension which is inclined with respect to an axis of extension of the said first tubular connecting element.

16. The device of Claim 12 and to any one of Claims 4 to 11, characterised in that the said hydrophilic membrane (16) is interpositioned between the said base (25) and the said cover portion (26), and extends throughout the said containing body (11).

17. The device of Claims 12 and of any one of Claims 4 to 11, characterised in that each of the said base (25) and the said cover portion (26) comprises a corresponding base wall (25a; 26a) and a corresponding perimeter edge (25b; 26b) emerging from the said base wall, the said hydrophilic membrane (16) extending parallel to the said base walls (25a; 26a) and distanced there-from.

18. The device of Claim 17, characterised in that the said containing body has a plurality of projections (31) emerging from the said base wall of the said base.

19. The device of Claim 17 or 18, characterised in that the said containing body has a plurality of projections (32) emerging from the said base wall of the said cover portion.

20. The device of Claim 18 or 19, characterised in that the said base projections (31) comprise teeth distributed uniformly over the surface of the said base wall of the said base.

21. The device of Claim 19 or 20, characterised in that the said cover portion projections (32) comprise deflectors spaced angularly to guide a flow of liquid towards the said first outlet.

22. The device of Claim 11, characterised in that the said first and second lateral portion (20, 22) are rigidly connected by a rigid cross-piece (23).

23. The device of Claims 22 and 12, characterised in that the said base (25) of the said containing body, the said rigid cross-piece (23) and the said second lateral portion (22) are made in a single piece.

24. The device of Claim 22 or 23, characterised in that the said rigid cross-piece is essentially flat and parallel to a lie plane of the said first length of tubing.

25. The device of any one of Claims 1 to 24, characterised in that the said control unit (8) is capable of performing an appropriate end of infusion procedure when an end of infusion condition is detected.

26. The device of Claim 25, characterised in that the said end of infusion procedure comprises a stage of commanding the said movement means (9) to stop transport of said fluid along the said line.

27. The device of Claim 25, characterised in that the said end of infusion procedure comprises a stage of signalling that the end of infusion condition has been reached.

28. The device of any one of Claims 1 to 27, characterised in that it comprises a plurality of the said containers (4), the said transport line (2) exhibiting a plurality of branches for fluid connection of each container to the said infusion point, and a corresponding flow shut-off element (6) acting on each of the said branches.

29. The device of Claim 28, characterised in that the said control unit (8) is capable of performing an appropriate end of infusion procedure when the end of infusion condition is detected, the said end of infusion procedure comprising the stage of commanding the opening of a shut-off element (6) associated with a container which is not empty.

30. The device of any one of the preceding claims, characterised in that it comprises at least one check valve (36), predisposed on the said transport line (2) to prevent a flow which is inverse to an infusion direction.

31. The device of claim 30, characterised in that the said check valve (36) is arranged between the said continuous fluid separator (10) and the said infusion point (5).

32. The device of claim 31, characterised in that the said check valve (36) is arranged immediately downstream of the said continuous fluid separator (10).

33. The device of claim 30 and of claim 8, characterised in that the said check valve (36) is an integral part of the said rigid support (1).

34. The device of claim 30 and of claim 2, characterised in that the said check valve (36) is arranged internally of the said containing body (11) in a zone comprised between the said selector means (15) and the said first outlet (13).

35. The device of claim 30, characterised in that the said check valve (36) comprises a mobile obturator organ (37), which operates on a passage mouth (35) of the said liquid portion.

36. The device of claim 35 and of claim 12, characterised in that the said passage mouth (35) is associated to the said cover portion (26) of the said containing body (11).

37. The device of claim 36, characterised in that the said cover portion (26) comprises a base wall (26a) and wherein the said selector means (15) comprise at least one hydrophilic membrane (16) facing and distanced from the said base

wall (26a), the said passage mouth (35) being associated to the said base wall (26a).

38. The device of claim 5, characterised in that the said containing body (11) internally defines a fluid passage (27) between the said separator inlet (12) and the said first outlet (13), the said hydrophobic membrane (17) being situated in an upper zone of a fluid passage portion (27a) located upstream of the said hydrophilic membrane (16), the said hydrophobic membrane (17) facing upwards in a use configuration of the said support element (1).

39. The device of claim 38, characterised in that the said upstream passage portion (27a) for fluid passage has at least one passage section which progressively increases in a direction towards the said hydrophobic membrane (17).

40. The device of claim 39, characterised in that the said hydrophobic membrane (17) is located superiorly with respect to an upper point of the operative surface of the said hydrophilic membrane (16).

41. The device of claim 11, characterised in that the said containing body (11) has a development which is prevalently in a transversal direction proceeding from the said first lateral portion (20) to the said second lateral portion (22), the said first outlet (13) being located in a lateral end zone of the said transversal development, in proximity of the said second lateral portion (22).

42. The device of claim 41, characterised in that the said second outlet (14) is arranged in an intermediate zone of the said transversal development.

43. An infusion device for medical use, comprising:

- at least one container (4) designed to hold a specified quantity of a fluid to be infused into a patient;

- a transport line (2) connected to the said container to convey the said fluid, in operating conditions, in an infusion direction leading from the said container (4) towards an infusion point (5);

- at least one continuous fluid separator (10), operating on the said transport line (2) and separating the said fluid into a gaseous portion and a liquid portion;
- at least one check valve (36), operating on the said transport line (2) for preventing a flow in an inverse direction to the said infusion direction;
- a rigid containing body (11) having at least one inlet (12) and at least a first outlet (13) for a fluid, inserted in the said transport line (2), which containing body (11) contains the said separator (10) and the said check valve (36), both of which separator (10) and check valve (36) are arranged between the said at least one inlet (12) and the said at least one outlet (13).

44. The device of claim 43, characterised in that the said continuous fluid separator (10) is the separator of any one of claims from 2 to 5 and from 12 to 21.

45. The device of claim 44, characterised in that the said check valve (36) is arranged internally of the said containing body (11) in a zone comprised between the said selector means (15) and the said first outlet (13).

46. The device of claim 43, characterised in that the said check valve (36) comprises a mobile obturating organ (37) operating on a passage mouth (35) of the said liquid portion.

47. The device of claim 44, characterised in that the said passage mouth (35) is associated to the said cover portion (26) of the said containing body (11).

48. The device of claim 47, characterised in that the said cover portion (26) comprises a base wall (26a), and wherein the said selector means (15) comprise at least one hydrophilic membrane (16) which faces the said base wall (26a) and is distanced there-from, the said passage mouth (35) being associated to the said base wall (26a).

49. Apparatus for extracorporeal blood treatment, comprising a device according to any one of the preceding claims.

50. Apparatus according to Claims 49 and 15, characterised in that it comprises an extracorporeal circuit (33) and a blood treatment unit (34) positioned in the said circuit (33), the said second connecting element (30) being directly and removably connected to a connector of the said extracorporeal blood circuit (33) upstream or downstream of a blood treatment unit (34).

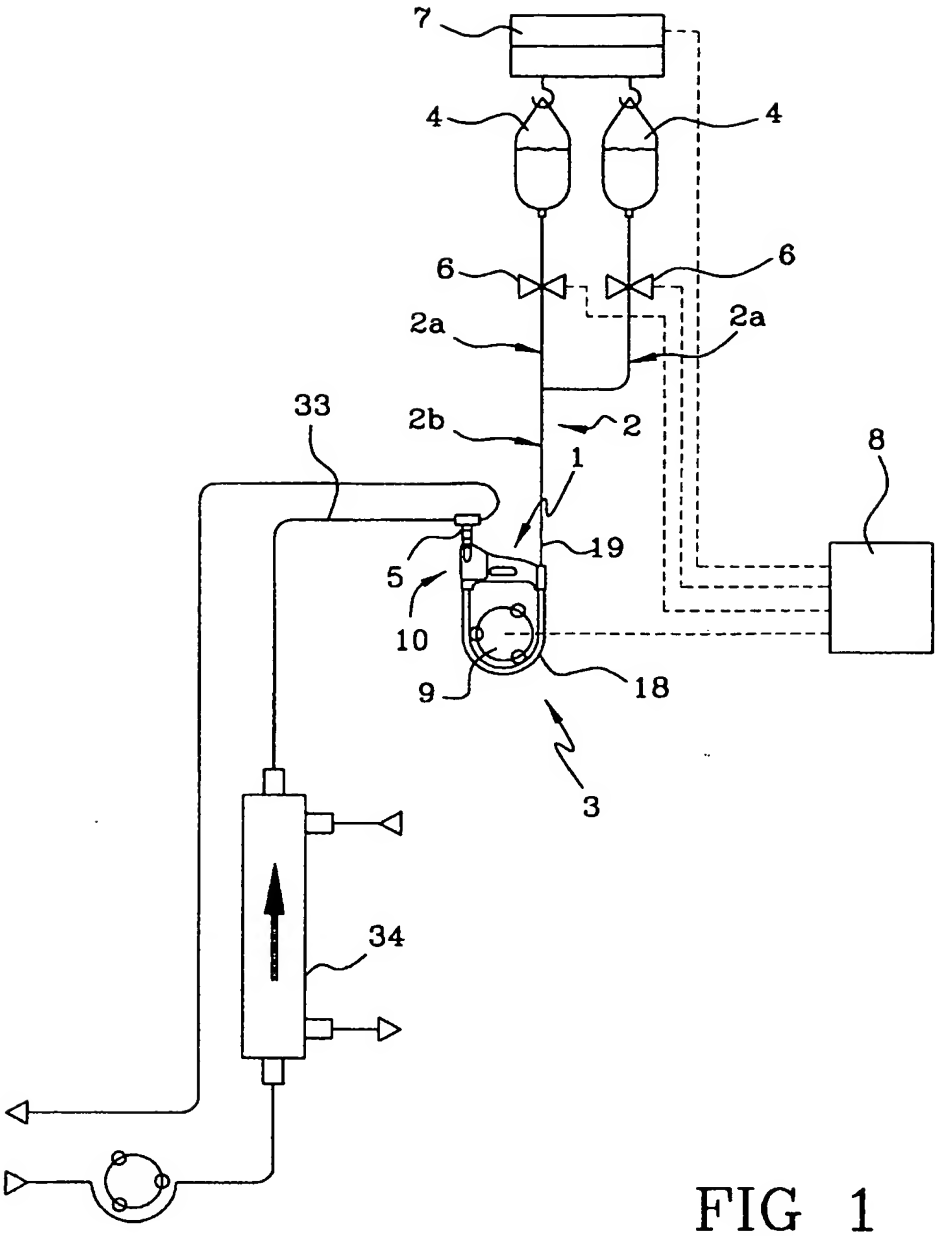


FIG 1

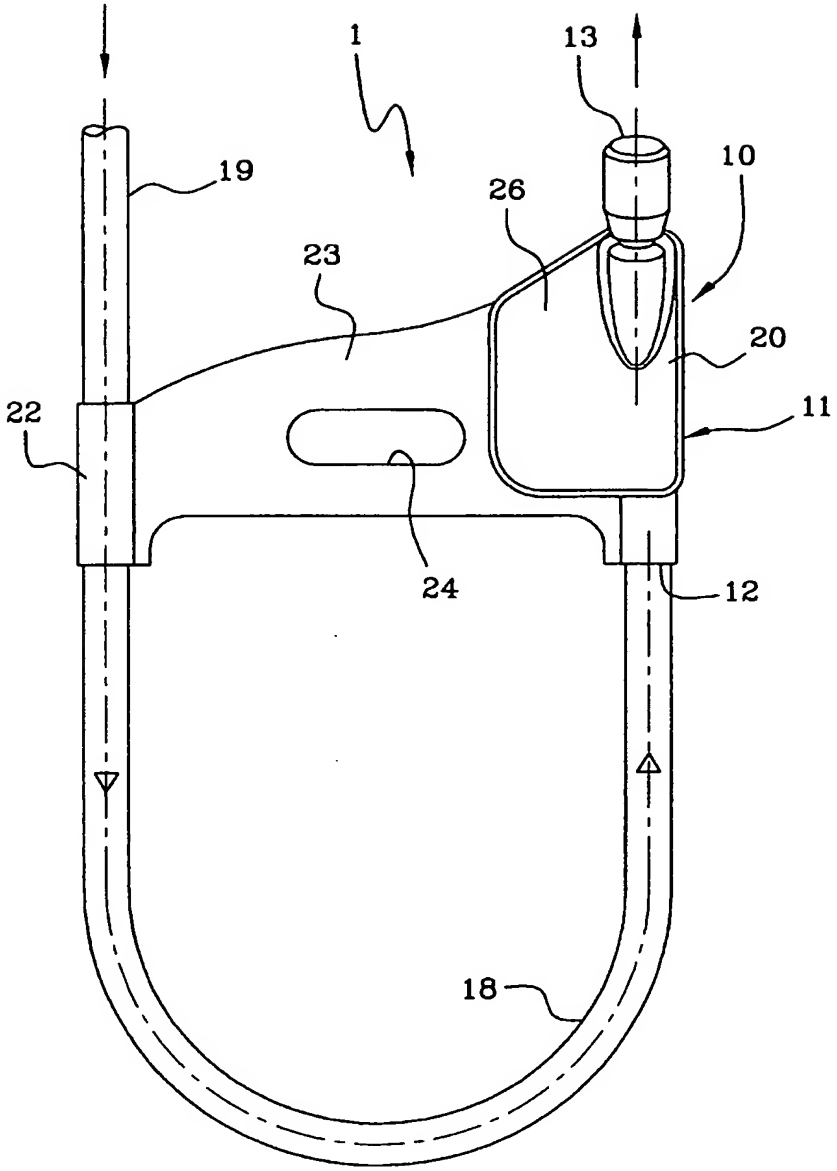


FIG 2

FIG 3

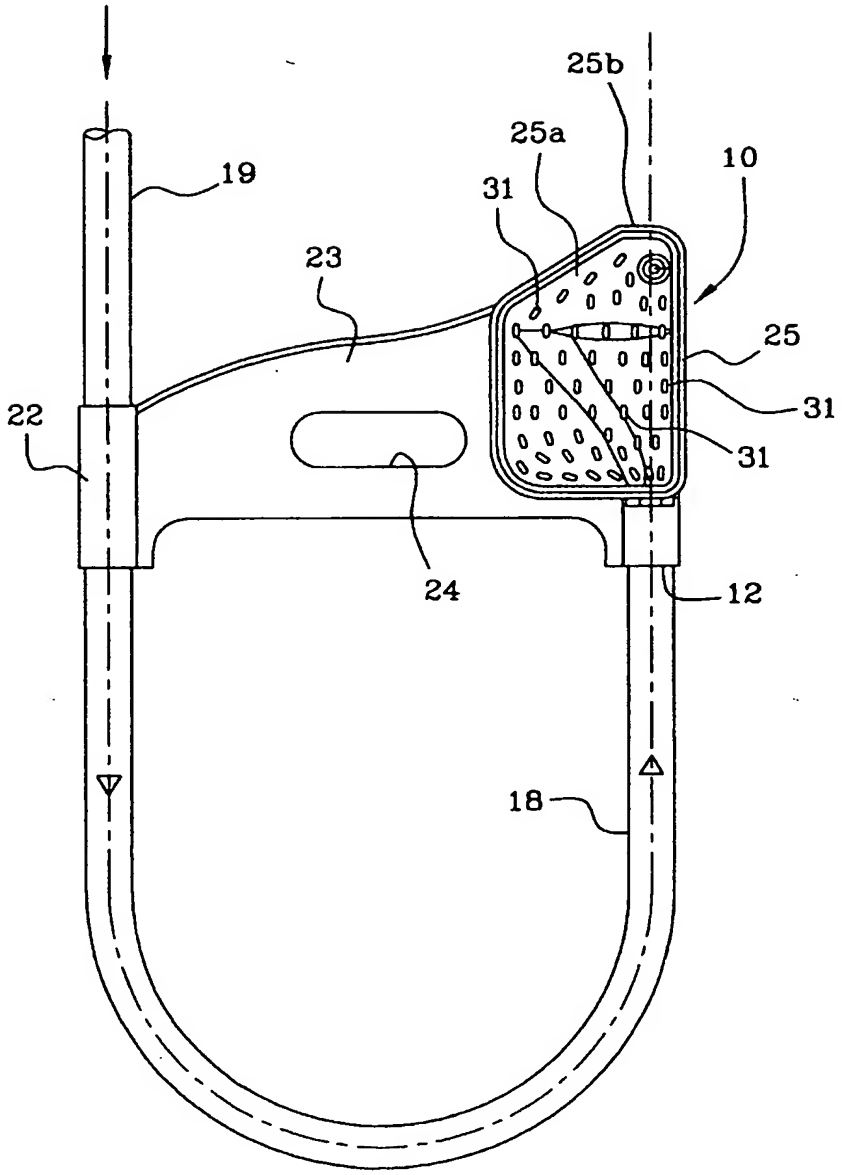
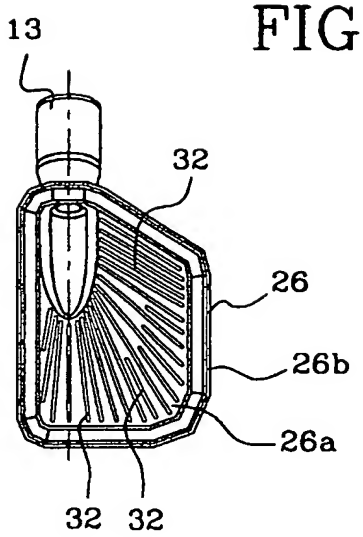


FIG 6



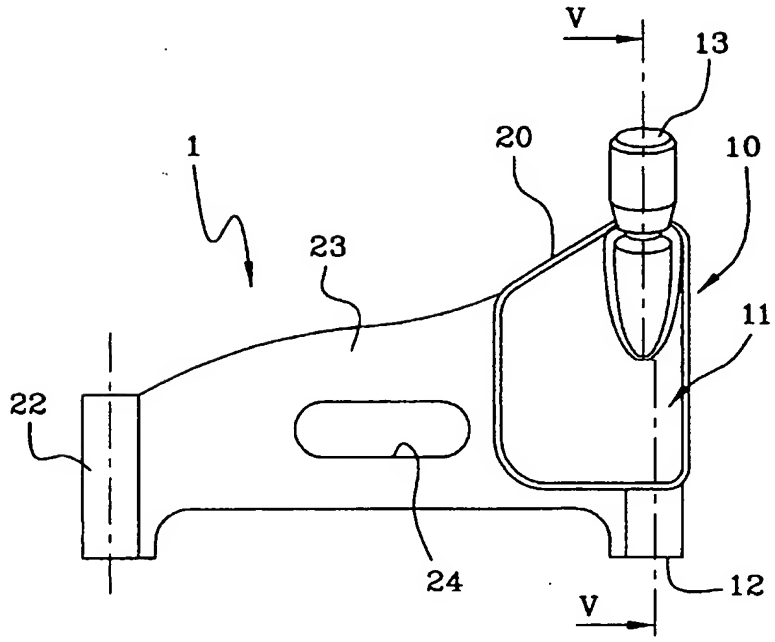


FIG 4

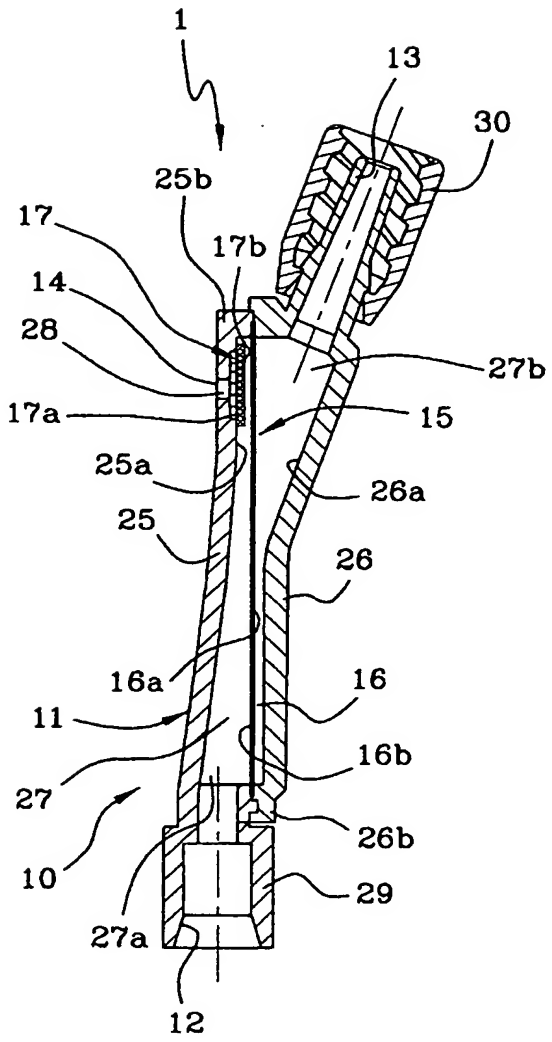

1
13
30
25b
17
17b
14
28
27b
17a
15
25a
26a
25
26
16a
16
11
16b
27
26b
10
29
27a
12

FIG 5

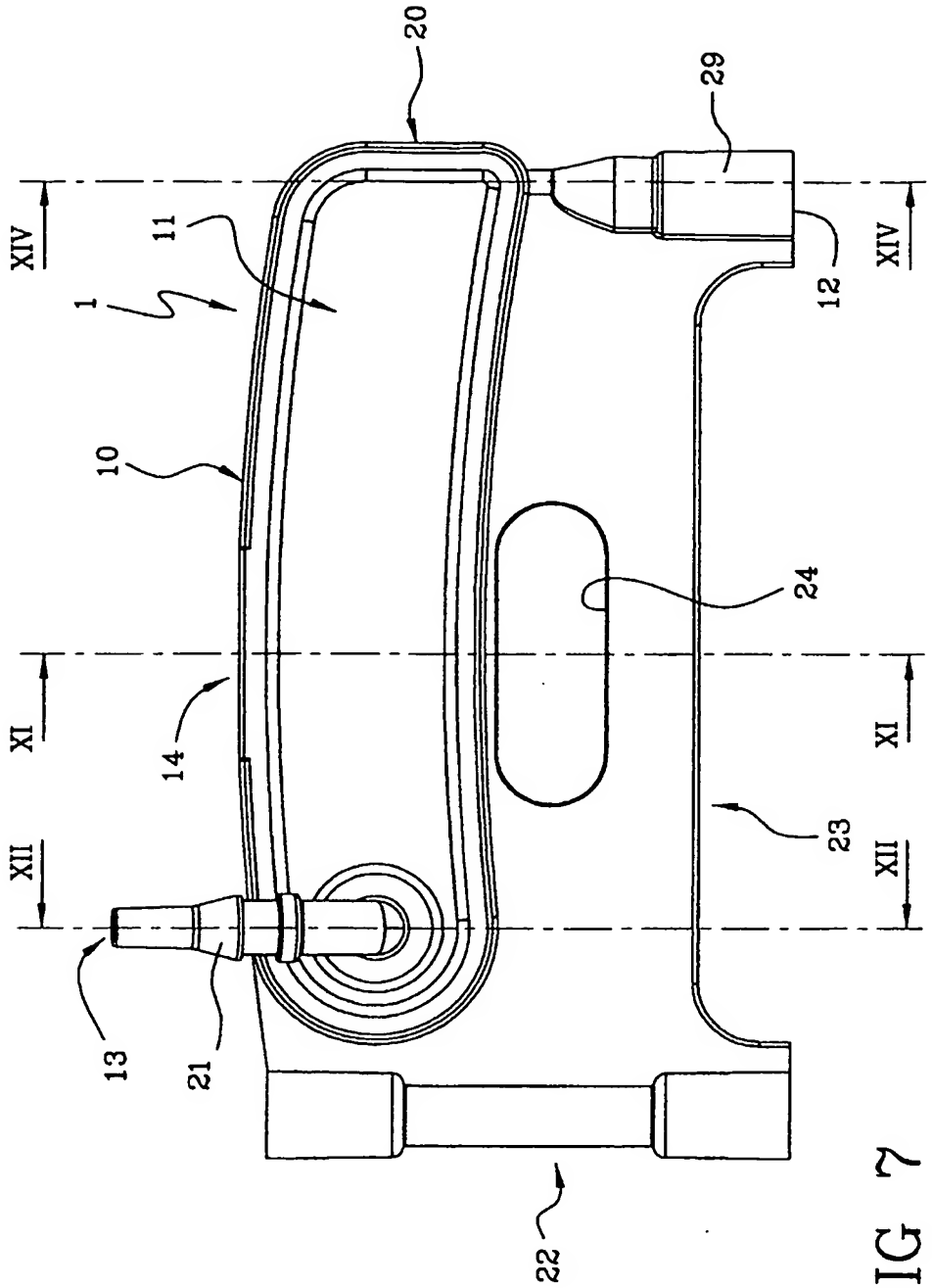


FIG 7

FIG 8

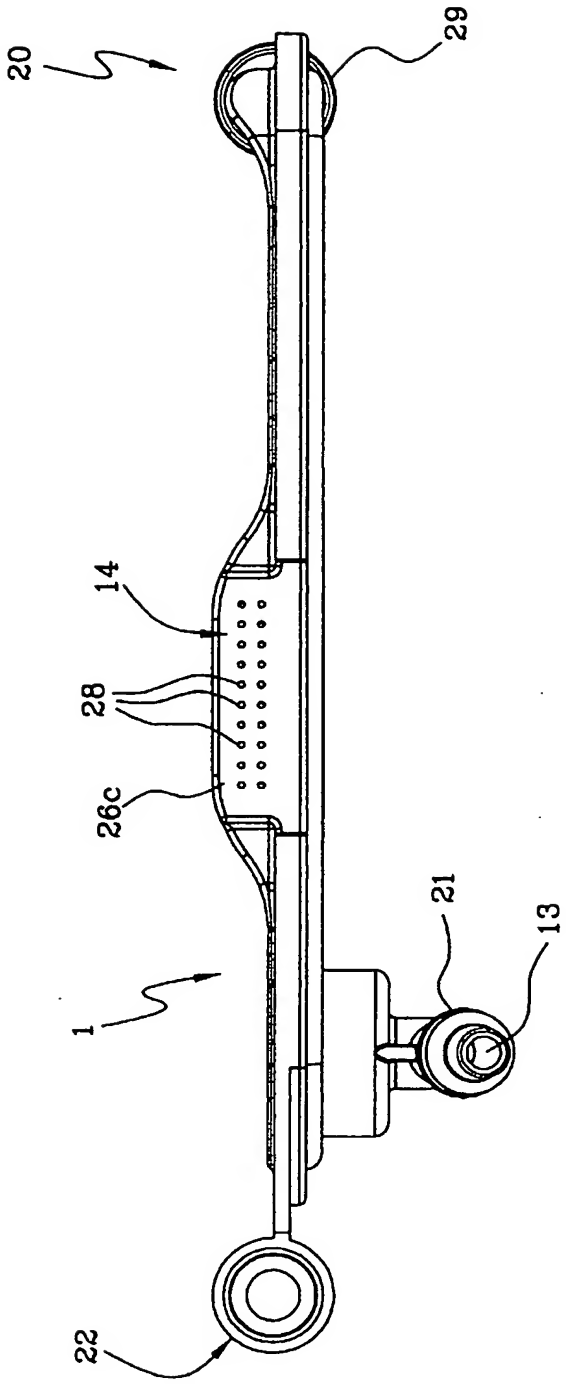
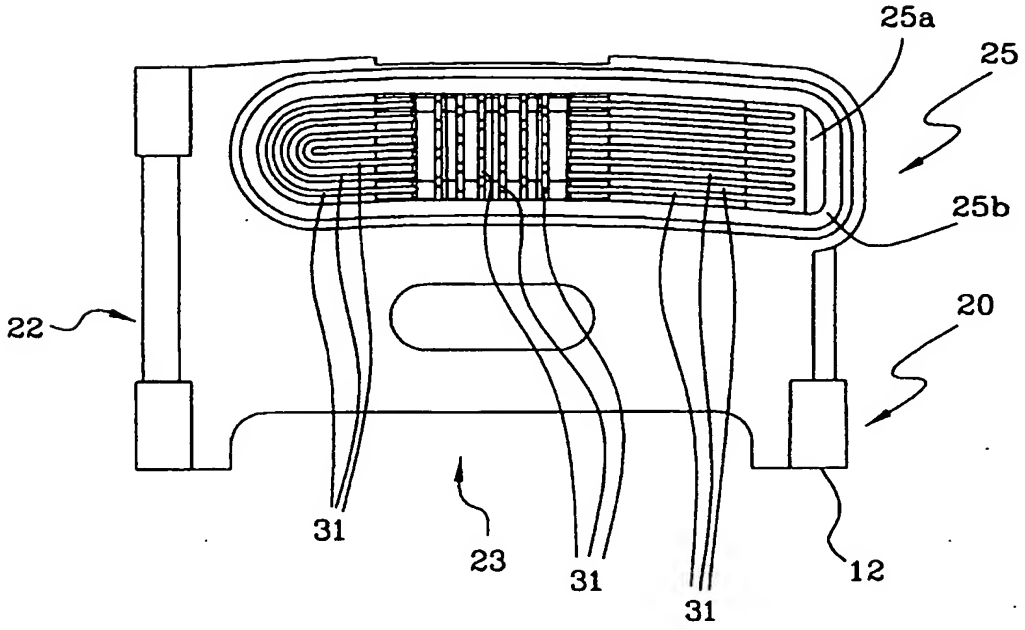


FIG 9



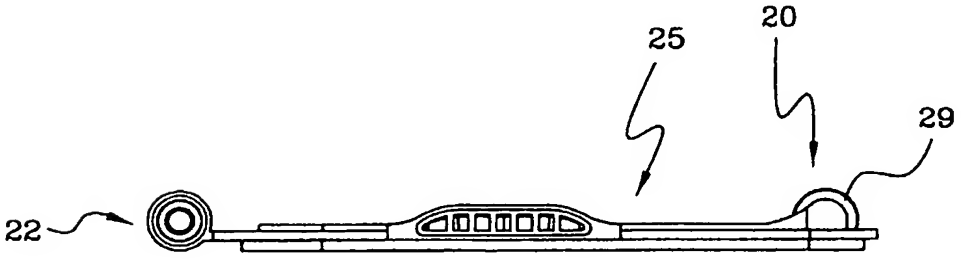


FIG 10

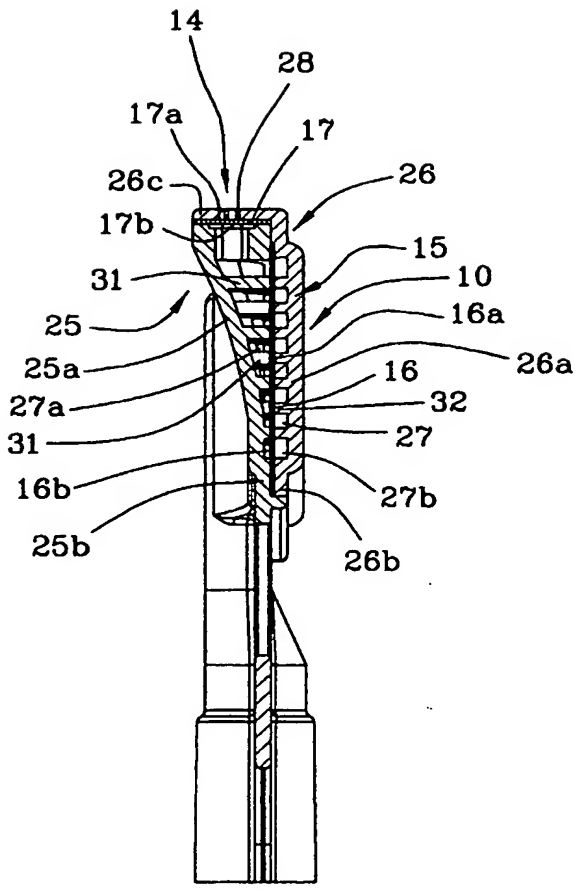

14
28
17a
17
26c
26
17b
15
31
10
25
16a
25a
26a
16
27a
32
31
27
16b
27b
25b
26b

FIG 11

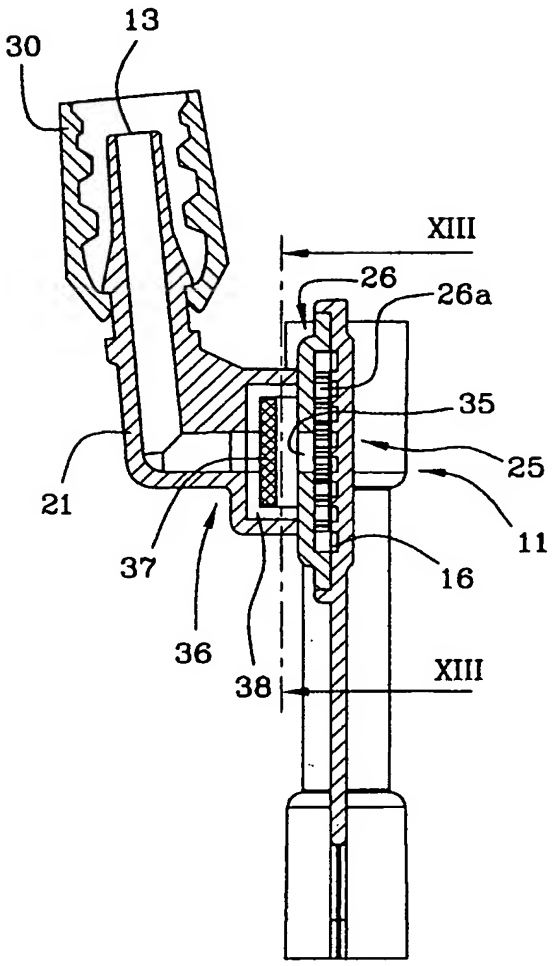


FIG 12

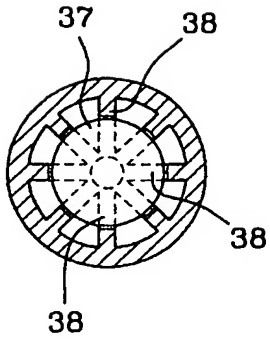


FIG 13

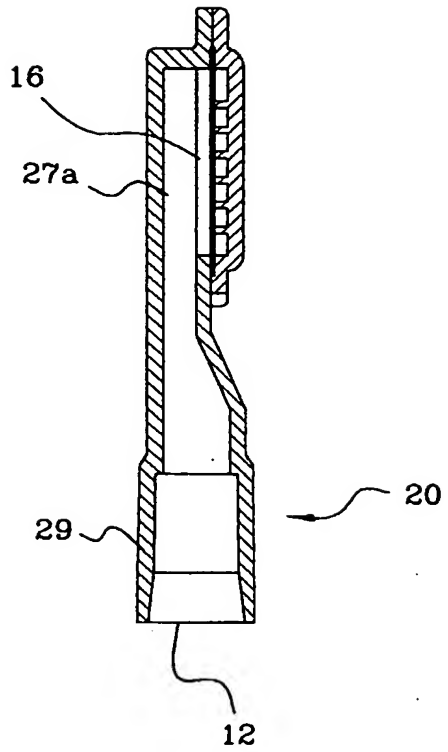


FIG 14

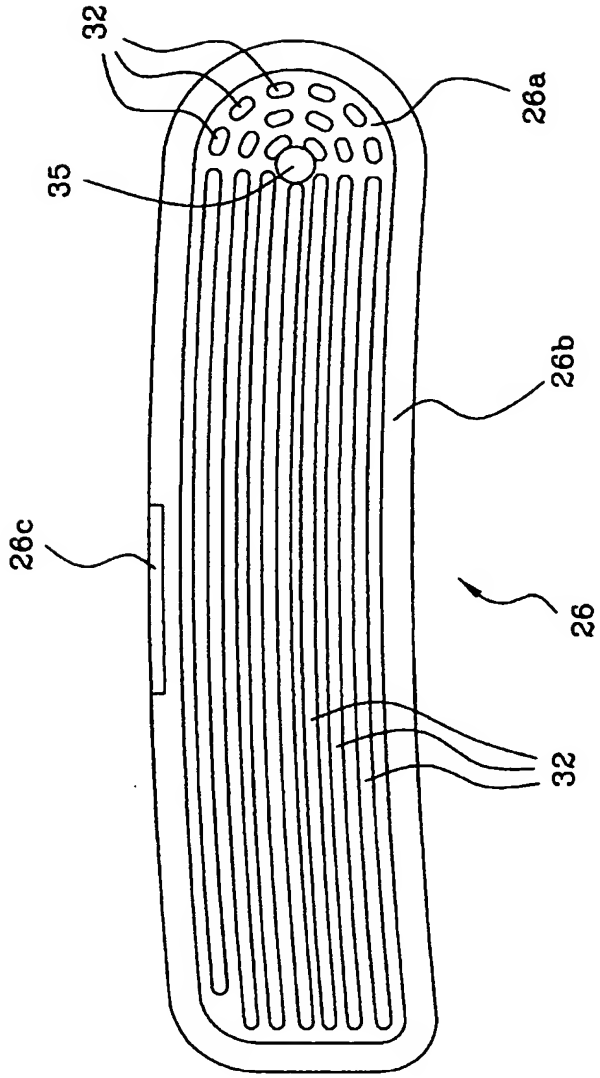


FIG 15

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT 21076Y	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/12456	International filing date *(day/month/year)* 08 April 2003 (08.04.2003)	Priority date *(day/month/year)* 12 April 2002 (12.04.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/439; C07D 221/22; A61P 35/00 and US Cl.: 514/295; 546/93		
Applicant MERCK & CO., INC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority

- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23 June 2003 (23.06.2003)	10 September 2004 (10.09.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Evelyn Huang Telephone No. 703-308-1235

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/12456

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-71 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 72-83, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/12456

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 3-5, 7-21	YES
	Claims 1, 2, 6	NO
Inventive Step (IS)	Claims 3-5, 7-21	YES
	Claims 1, 2, 6	NO
Industrial Applicability (IA)	Claims 1-21	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 2, 6 lack novelty under PCT Article 33(2) as being anticipated by US 4,332, 810. The compounds of Examples 1-5 and the composition thereof, are encompassed by the instant claims.

Claims 1, 2, 6 lack novelty under PCT Article 33(2) as being anticipated by BELANGER et al. The compounds 6, 8 (page 2177) and 11, 15 (page 2178) and the composition thereof, are encompassed by the instant claims.

Claims 1, 2 lack novelty under PCT Article 33(2) as being anticipated by IDDON et al. The compounds 24, 25 (page 1085) are encompassed by the instant claims.

Claims 2-5, 7-21 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instant $(CR^{1a}{}_2)_n$-X- $(CR^{1a}{}_2)_p$-V-$(R^2)_q$ substituent wherein n, p, q is not zero and V is not H.

Claims 1-21 meet the criteria set out in PCT Article 33(4), and thus find industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry as a tyrosine kinase inhibitor useful for treatment of a tyrosine kinase related disorder.

---------- NEW CITATIONS ----------